UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/677,662 | 10/02/2003 | Gideon Dreyfuss | 053893-5027-01 | 9955 |

23973 7590 01/09/2007

DRINKER BIDDLE & REATH
ATTN: INTELLECTUAL PROPERTY GROUP
ONE LOGAN SQUARE
18TH AND CHERRY STREETS
PHILADELPHIA, PA 19103-6996

| EXAMINER | |
|---|---|
| BUNNER, BRIDGET E | |
| **ART UNIT** | **PAPER NUMBER** |
| 1647 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 01/09/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/677,662 | DREYFUSS ET AL. | |
| | Examiner | Art Unit | |
| | Bridget E. Bunner | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *16 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *8-13 and 102-107* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-13 and 102-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02 October 2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Appendix A*.

## DETAILED ACTION

### *Status of Application, Amendments and/or Claims*

The amendment of 02 October 2003 has been entered in full. Claims 8 and 10-13 are amended. Claims 1-7 and 14-101 are cancelled. Claims 102-107 are added.

Claims 8-13 and 102-107 are under consideration in the instant application.

### *Drawings*

1. The revised formal drawings were received on 02 October 2003. These drawings are acceptable.

### *Specification*

2. The disclosure is objected to because of the following informalities:

2a. An updated status of the parent nonprovisional application should be included in the first sentence of the specification. A statement reading "This is a divisional of U.S. Application No. 09/399,081, filed September 17, 1999, Patent No. 6,646,113 which claims priority pursuant 35 U.S.C. § 119(e) to U.S. Provisional Application 60/100,866, filed on September 17, 1998" should be entered.

2b. The Brief Description of the Drawings does not refer to Figures 50A-H, Figures 51A-D, and Figures 52A-D.

2c. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "NUCLEIC ACID MOLECULE ENCODING SURVIVAL OF MOTOR NEURON-INTERACTING PROTEIN 1 (SIP1)".

Appropriate correction is required.

***Claim Rejections - 35 USC § 112, second paragraph***

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 10, 12, 102, 104, 106, and 107 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 107 is rejected as being indefinite because it is not clear how a mutation of SIP1 comprises both a deletion of the carboxyl terminal 89 amino acids relative to the amino acid sequence of SEQ ID NO: 2 and a deletion of the carboxyl terminal 162 amino acids relative to the amino acid sequence of SEQ ID NO: 2. (Please note that this issue could be overcome by amending claim 107, lines 4-5 to recite, for example, "...wherein said mutation is selected from the group consisting of a deletion of the carboxyl terminal 89 amino acids...".)

6. The term "specifying" in claims 10, 12, 102, 104 and 106 is a relative term which renders the claims indefinite. The term "specifying" is not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear what the term "specifying" encompasses or how a nucleic acid sequences "specifies" a promoter. For example, does it mean "encoding", "corresponding to", "representing", etc.? (Please note that this issue could be overcome by amending the claims to recite, for example "...said nucleic acid (or vector) further operably linked to a nucleic acid comprising a promoter/regulatory sequence".)

***Claim Rejections - 35 USC § 112, first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 8-13 and 102-106 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding a eukaryotic *SIP1*, wherein said nucleic acid comprises SEQ ID NO: 1 or SEQ ID NO: 3, said nucleic acid further comprising a nucleic acid encoding a tag polypeptide, *does not reasonably provide enablement for* an isolated nucleic acid encoding a eukaryotic *SIP1* and any mutants, derivatives, variants, and fragments thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are directed to an isolated nucleic acid encoding a eukaryotic survival of motor neuron-interacting protein 1 and any mutants, derivatives, variants, and fragments thereof, said nucleic acid further comprising a nucleic acid encoding a tag polypeptide covalently linked thereto. The claims are also directed to recombinant cells comprising the nucleic acid and vectors.

The specification of the instant application teaches nucleotide sequences encoding wild-type SIP1 and two SIP1 deletion mutants, SIP1ΔC89 and SIP1ΔC162 (Figure 1; Figure 45; pg 170, lines 1-10). However, the specification does not teach other "variants or recombinantly derived mutants of wild-type SIP1 DNA sequences, which variants render the protein encoded thereby either more, less, or just as biologically active as the full-length wild type SIP1 of the

invention" (pg 43, lines 1-4). Further, the specification discloses that the term "fragment" as applied to a nucleic acid "may ordinarily be at least about 20 nucleotides in length, typically at least 100, more typically, from about 100 to about 500 nucleotides, typically at least forty contiguous amino acids, preferably at least 500 to 1,000 nucleotides, even more preferably at least about 1,000 nucleotides to about 2,000 nucleotides, yet even more preferably at least about 2,000 to about 3,500, and most preferably, the nucleic acid fragment will be greater than about 3,500 nucleotides in length" (pg 92, lines 19-26). The specification does not teach nucleic acids encoding all possible SIP1 polypeptides, including mutants, derivatives, variants, and fragments, other than the full-length SIP1 nucleic acid sequences of SEQ ID NOs: 1 and 3 and the nucleic acid sequences encoding deletion mutants, SIP1ΔC89 and SIP1ΔC162. The specification also does not teach functional or structural characteristics of the nucleic acids encoding all possible SIP1 polypeptide mutants, derivatives, variants, and fragments recited in the claims.

The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein

Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

Additionally, the Examiner has interpreted claims 11-12 and 105-106 as reading on isolated host cells, as well as host cells in the context of a multicellular, transgenic organism and host cells intended for gene therapy. The specification of the instant application teaches that when the recombinant cell is a eukaryotic cell, the transgene of the invention is introduced therein (pg 58, lines 18-31). The specification teaches that a system has been provided wherein

the expression of the desired gene can be studied *in vitro* in the laboratory or in a mammal (pg 59, lines 1-7). However, there are no methods or working examples disclosed in the instant application whereby a multicellular animal with incorporated SIP1 nucleic acids is demonstrated to express any SIP1 polypeptide. There are also no methods or working examples in the specification indicating that a multicellular animal has SIP1 "knocked out". The unpredictability of the art is *very high* with regards to making transgenic animals. For example, Wang et al. (Nuc. Acids Res. 27: 4609-4618, 1999; pg 4617) surveyed gene expression in transgenic animals and found in each experimental animal with a single "knock-in" gene, multiple changes in genes and protein products, often many of which were unrelated to the original gene. Likewise, Kaufman et al (Blood 94: 3178-3184, 1999) found transgene expression levels in their transfected animals varied from "full" (9 %) to "intermediate" to "none" due to factors such as "vector poisoning" and spontaneous structural rearrangements (pg 3180, col 1, 2$^{nd}$ full paragraph; pg 3182-3183).

The specification also discloses that nucleic acids encoding SIP1 polypeptides can be used for gene therapy (pg 50, lines 16-21; pg 58, lines 21-24; pg 59, lines 1-5). However, the specification does not teach any methods or working examples that indicate a SIP1 nucleic acid is introduced and expressed in a cell for therapeutic purposes. The disclosure in the specification is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. For example, the specification does not teach what type of vector would introduce the SIP1 nucleic acid into the cell or in what quantity and duration. Relevant literature teaches that since 1990, about 3500 patients have been treated via gene therapy and although some evidence of gene transfer has been seen, it has generally been inadequate for a meaningful

clinical response (Phillips, A., J Pharm Pharmacology 53: 1169-1174, 2001; abstract). Additionally, the major challenge to gene therapy is to deliver DNA to the target tissues and to transport it to the cell nucleus to enable the required protein to be expressed (Phillips, A.; pg 1170, ¶ 1). Phillips also states that the problem with gene therapy is two-fold: 1) a system must designed to deliver DNA to a specific target and to prevent degradation within the body, and 2) an expression system must be built into the DNA construct to allow the target cell to express the protein at therapeutic levels for the desired length of time (pg 1170, ¶ 1). Therefore, undue experimentation would be required of the skilled artisan to introduce and express a SIP1 nucleic acid into the cell of an organism. Additionally, gene therapy is unpredictable and complex wherein one skilled in the art may not necessarily be able to introduce and express a SIP1 nucleic acid in the cell of an organism or be able to produce a SIP1 protein in that cell. (Please note that this issue could be overcome by amending the claims to recite, for example, "An isolated cell...").

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen the same for activity, and to generate a transgenic animal expressing a SIP1 protein and to introduce and express a SIP1 nucleic acid in a cell of an organism for therapy; the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity and how to introduce a SIP1 nucleic acid in the cell of an organism to be able produce that SIP1; the absence of working examples directed to same; the complex nature of the invention; the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function and the unpredictability of making transgenic animals and of transferring genes into an

organism's cells; and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

8. Claims 8-13 and 102-106 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed to an isolated nucleic acid encoding a eukaryotic survival of motor neuron-interacting protein 1 and any mutants, derivatives, variants, and fragments thereof, said nucleic acid further comprising a nucleic acid encoding a tag polypeptide covalently linked thereto. The claims are also directed to recombinant cells comprising the nucleic acid and vectors. The claims do not require that the polypeptides encoded by the nucleic acids possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of nucleic acids.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, there is not even identification of

any particular portion of the structure or function that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. Additionally, the description of two wild-type SIP1 polynucleotide species (SEQ ID NOs: 1, 3) and two polynucleotide species encoding SIP1 deletion mutants (SIP1ΔC89 and SIP1ΔC162) is not adequate written description of an entire genus of functionally equivalent polynucleotides which incorporate all mutants, derivatives, variants and fragments of any SIP1 nucleic acid.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

The skilled artisan cannot envision the detailed chemical structure of the encompassed nucleic acid molecules, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to

lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an isolated nucleic acid molecule comprising the nucleic acid sequence of SEQ ID NO:1 (human) or SEQ ID NO: 3 (*Xenopus*) or isolated nucleic acid molecules encoding mutant SIP1ΔC89 and mutant SIP1ΔC162, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 8-13 and 102-106 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (Genbank Accession No. AF027150, 30 October 1997) in view of Uckun et al. (U.S. Patent 6,160,010).

Liu et al. teach an isolated nucleic acid sequence that is 100% identical to the nucleic acid sequence of SEQ ID NO: 1 of the instant application (see sequence alignment attached to the instant Office Action as Appendix A). Liu et al. also disclose that the nucleic acid encodes a survival of motor neuron interacting protein 1 (SIP1).

Liu et al. do not teach the SIP1 nucleic acid further comprises a nucleic acid encoding a tag polypeptide. Liu et al. also do not teach that the nucleic acid further comprises a promoter/regulatory sequence operably linked thereto. Liu et al. does not disclose a vector comprising the nucleic acid or a recombinant host cell (such as a pre-B lymphoid DT40 cell).

Uckun et al. teach that cDNAs encoding full length Bruton's tyrosine kinase (BTK) and its kinase or PH domains are cloned into the *E. coli* expression vector pMALC2 with the IPTG-inducible ptac promoter to create a fusion between these coding sequences and the 3' end of the *E. coli* malE gene, which codes for maltose binding protein (col 19, lines 7-14). Uckun et al. also disclose that cDNAs encoding the SH2, SH3, or SH2+SH3 domains of BTK are cloned into the *E. coli* expression vector pGEX-2t with the IPTG-inducible ptac promoter to create a fusion between these coding sequences and the 3' end of the *E. coli* glutathione S-transferase (GST) gene (col 19, lines 14-19). Furthermore, Uckun et al. teach that DT40 cells are transfected with BTK-MBP DNA (col 19, lines 45-51; col 20, lines 34-60).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the SIP1 nucleic acid sequence of Liu et al. by generating a tag

fusion nucleic acid and expression system as taught by Uckun et al. The person of ordinary skill in the art would have been motivated to make that modification to allow for the expression of the SIP1 polynucleotide and subsequent isolation, identification, or localization of the protein of interest. The person of ordinary skill in the art reasonably would have expected success because similar vector-host cell systems and tag-nucleic acid fusions were already being generated using other protein sequences at the time the invention was made. Therefore, the claimed invention as a whole was clearly *prima facie* obvious over the prior art.

***Conclusion***

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (571) 272-0881. The examiner can normally be reached on 8:30-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BEB
Art Unit 1647
27 December 2006

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER

Appendix A

```
<!--StartFragment-->RESULT 2
AF027150
LOCUS       AF027150                1285 bp    mRNA    linear   PRI 30-OCT-1997
DEFINITION  Homo sapiens survival of motor neuron protein interacting protein 1
            (SIP1) mRNA, complete cds.
ACCESSION   AF027150
VERSION     AF027150.1  GI:2570924
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1  (bases 1 to 1285)
  AUTHORS   Liu,Q., Fischer,U., Wang,F. and Dreyfuss,G.
  TITLE     The spinal muscular atrophy disease gene product, SMN, and its
            associated protein SIP1 are in a complex with spliceosomal snRNP
            proteins
  JOURNAL   Cell 90 (6), 1013-1021 (1997)
   PUBMED   9323129
REFERENCE   2  (bases 1 to 1285)
  AUTHORS   Fischer,U., Liu,Q. and Dreyfuss,G.
  TITLE     The SMN-SIP1 complex has an essential role in spliceosomal snRNP
            biogenesis
  JOURNAL   Cell 90 (6), 1023-1029 (1997)
   PUBMED   9323130
REFERENCE   3  (bases 1 to 1285)
  AUTHORS   Liu,Q. and Dreyfuss,G.
  TITLE     Direct Submission
  JOURNAL   Submitted (29-SEP-1997) Howard Hughes Medical Inst., University of
            Pennsylvania, 415 Curie Blvd., Philadelphia, PA 19104, USA
FEATURES             Location/Qualifiers
     source          1. .1285
                     /organism="Homo sapiens"
                     /mol_type="mRNA"
                     /db_xref="taxon:9606"
                     /cell_line="HeLa"
     gene            1. .1285
                     /gene="SIP1"
     CDS             84. .926
                     /gene="SIP1"
                     /note="SMN protein interacting protein 1"
                     /codon_start=1
                     /product="survival of motor neuron protein interacting
                     protein 1"
                     /protein_id="AAB82297.1"
                     /db_xref="GI:2570925"
                     /translation="MRRAELAGLKTMAWVPAESAVEELMPRLLPVEPCDLTEGFDPSV
                     PPRTPQEYLRRVQIEAAQCPDVVVAQIDPKKLKRKQSVNISLSGCQPAPEGYSPTLQW
                     QQQQVAQFSTVRQNVNKHRSHWKSQQLDSNVTMPKSEDEEGWKKFCLGEKLCADGAVG
                     PATNESPGIDYVQIGFPPLLSIVSRMNQATVTSVLEYLSNWFGERDFTPELGRWLYAL
                     LACLEKPLLPEAHSLIRQLARRCSEVRLLVDSKDDERVPALNLLICLVSRYFDQRDLA
                     DEPS"
ORIGIN

  Query Match          100.0%;  Score 1284;  DB 5;  Length 1285;
  Best Local Similarity   100.0%;  Pred. No. 0;
  Matches 1285;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 TAACGCTCCCTAAACTGCCACTTGNTCAGCTCCGCGCCTAAGGTGTCTATTAGTGCGCCT 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 TAACGCTCCCTAAACTGCCACTTGNTCAGCTCCGCGCCTAAGGTGTCTATTAGTGCGCCT 60

Qy         61 GCGCTGTGACCTAGAATGGGCGCATGCGCCGAGCGGAACTGGCTGGTTTGAAAACCATGG 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 GCGCTGTGACCTAGAATGGGCGCATGCGCCGAGCGGAACTGGCTGGTTTGAAAACCATGG 120

Qy        121 CGTGGGTACCAGCGGAGTCCGCAGTGGAAGAGTTGATGCCTCGGCTATTGCCGGTAGAGC 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 CGTGGGTACCAGCGGAGTCCGCAGTGGAAGAGTTGATGCCTCGGCTATTGCCGGTAGAGC 180

Qy        181 CTTGCGACTTGACGGAAGGTTTCGATCCCTCGGTACCCCCGAGGACGCCTCAGGAATACC 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 CTTGCGACTTGACGGAAGGTTTCGATCCCTCGGTACCCCCGAGGACGCCTCAGGAATACC 240

Qy        241 TGAGGCGGGTCCAGATCGAAGCAGCTCAATGTCCAGATGTTGTGGTAGCTCAAATTGACC 300
```

Appendix A (cont.)

```
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 TGAGGCGGGTCCAGATCGAAGCAGCTCAATGTCCAGATGTTGTGGTAGCTCAAATTGACC 300

Qy        301 CAAAGAAGTTGAAAAGGAAGCAAAGTGTGAATATTTCTCTTTCAGGATGCCAACCCGCCC 360
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 CAAAGAAGTTGAAAAGGAAGCAAAGTGTGAATATTTCTCTTTCAGGATGCCAACCCGCCC 360

Qy        361 CTGAAGGTTATTCCCCAACACTTCAATGGCAACAGCAACAAGTGGCACAGTTTTCAACTG 420
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 CTGAAGGTTATTCCCCAACACTTCAATGGCAACAGCAACAAGTGGCACAGTTTTCAACTG 420

Qy        421 TTCGACAGAATGTGAACAAACATAGAAGTCACTGGAAATCACAACAGTTGGATAGTAATG 480
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        421 TTCGACAGAATGTGAACAAACATAGAAGTCACTGGAAATCACAACAGTTGGATAGTAATG 480

Qy        481 TGACAATGCCAAAATCTGAAGATGAAGAAGGCTGGAAGAAATTTTGTCTGGGTGAAAAGT 540
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 TGACAATGCCAAAATCTGAAGATGAAGAAGGCTGGAAGAAATTTTGTCTGGGTGAAAAGT 540

Qy        541 TATGTGCTGACGGGGCTGTTGGACCAGCCACAAATGAAAGTCCTGGAATAGATTATGTAC 600
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        541 TATGTGCTGACGGGGCTGTTGGACCAGCCACAAATGAAAGTCCTGGAATAGATTATGTAC 600

Qy        601 AAATTGGTTTTCCTCCCTTGCTTAGTATTGTTAGCAGAATGAATCAGGCAACAGTAACTA 660
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        601 AAATTGGTTTTCCTCCCTTGCTTAGTATTGTTAGCAGAATGAATCAGGCAACAGTAACTA 660

Qy        661 GTGTCTTGGAATATCTGAGTAATTGGTTTGGAGAAAGAGACTTTACTCCAGAATTGGGAA 720
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        661 GTGTCTTGGAATATCTGAGTAATTGGTTTGGAGAAAGAGACTTTACTCCAGAATTGGGAA 720

Qy        721 GATGGCTTTATGCTTTATTGGCTTGTCTTGAAAAGCCTTTGTTACCTGAGGCTCATTCAC 780
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        721 GATGGCTTTATGCTTTATTGGCTTGTCTTGAAAAGCCTTTGTTACCTGAGGCTCATTCAC 780

Qy        781 TGATTCGGCAGCTTGCAAGAAGGTGCTCTGAAGTGAGGCTCTTAGTGGATAGCAAAGATG 840
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        781 TGATTCGGCAGCTTGCAAGAAGGTGCTCTGAAGTGAGGCTCTTAGTGGATAGCAAAGATG 840

Qy        841 ATGAGAGGGTTCCTGCTTTGAATTTATTAATCTGCTTGGTTAGCAGGTATTTTGACCAAC 900
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        841 ATGAGAGGGTTCCTGCTTTGAATTTATTAATCTGCTTGGTTAGCAGGTATTTTGACCAAC 900

Qy        901 GTGATTTAGCTGATGAGCCATCTTGATGTAGCTGATCTCTCAGGGATAGAAGATATTTCT 960
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        901 GTGATTTAGCTGATGAGCCATCTTGATGTAGCTGATCTCTCAGGGATAGAAGATATTTCT 960

Qy        961 CATGAAGGCAGCCTAACTCTGAGGAAAACAATGCCAATTCAAGTACAGATTTCAACACAT 1020
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        961 CATGAAGGCAGCCTAACTCTGAGGAAAACAATGCCAATTCAAGTACAGATTTCAACACAT 1020

Qy       1021 CTTCAACACTATGTGAAGGGTTCACATCTTAACCTGTGCAATTCAGATTGATACTCAGAA 1080
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1021 CTTCAACACTATGTGAAGGGTTCACATCTTAACCTGTGCAATTCAGATTGATACTCAGAA 1080

Qy       1081 TATGGGTTGATTTGAATATCTGAAATATCAATGGAAAATCCCACTCAGTTTTTGATGAAC 1140
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1081 TATGGGTTGATTTGAATATCTGAAATATCAATGGAAAATCCCACTCAGTTTTTGATGAAC 1140

Qy       1141 AGTTTGAACAGTTTTCTGTAATCAAGCAGCTTGCATAGAAATTGTATGATGAAATTTTAC 1200
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1141 AGTTTGAACAGTTTTCTGTAATCAAGCAGCTTGCATAGAAATTGTATGATGAAATTTTAC 1200

Qy       1201 ATAGGTTCTTGGTGCTGTTTTGTTCTTTTTTTGTTTTTTGTTGTTTTGTTATTTACTTAT 1260
                ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1201 ATAGGTTCTTGGTGCTGTTTTGTTCTTTTTTTGTTTTTTGTTGTTTTGTTATTTACTTAT 1260

Qy       1261 ATACATATAAAATTTTATTGAAAAT 1285
                |||||||||||||||||||||||||
Db       1261 ATACATATAAAATTTTATTGAAAAT 1285
<!--EndFragment-->
```